REMARKS

Claims 221-225, 232-239, 241-245, 247-248 and 250-251 are currently pending in the application. Claim 249 has been cancelled without prejudice. Claims 221, 224, 232, 235, 237 and 249 are amended. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Applicants thank Examiner Whiteman very much for his time in discussing claim amendments on January 6, 2003, and for his consideration of this after-final amendment.

In light of the brief discussion, the four base claims (Claims 221, 224, 232 and 237) have been amended to more clearly differentiate the claimed invention from the cited art.

Objection to the Claims

The Office Action states that Claims 241-242, 244 and 247 are free of the prior art, but are objected to as being dependent upon a rejected base claim (Claim 221). Applicants have amended the base claim to place it in condition for allowance, as discussed below, thereby obviating this objection.

IDS

The Office Action states that the patent (DE 196 18 797 C2) filed in the information disclosure statement filed 10/27/03 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of its relevance, and has not been considered.

Applicants note that a copy of this patent, which is not in the English language, and a concise explanation of its relevance, was filed in an IDS filed in the spring of 2002, (Paper No. 19 or 20), and has already been considered by the examiner to the extent of an abstract.

Claim Rejections –35 USC 112

Claim 249 was rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 249 has been cancelled and therefore the rejection is moot.

Claim Rejections – 35 U.S.C. § 102

Claims 221, 223-224 and 249 were rejected under 102(b) as being anticipated by Alfonzo et al. (Nucleic Acid Research, Vol. 25, 3751-3759, 1997).

The Office action states that "the term 'comprising' and 'having' means that any dsRNA that comprises a region that is complementary to an RNA transcript of a mammalian gene and the region is not more than 49 nucleotides anticipates the claimed product". Applicants have amended the base claims 221 and 224, to recite that the encompassed oligoribonucleotide consists of a dsRNA. Claim 249 has been cancelled by Applicants because it does not further limit newly amended claim 221.

Applicants submit that by substituting the closed language of "consists of" or "consisting of" in place of the open language of "having" or "comprising" in the recitation of the dsRNA of the oligoribonucleotide of the instant claims, precludes the instant claims from being anticipated by Alfonzo et al.

Applicants note that the structure of the in vivo duplex taught by Alfonzo et al. is ambiguous as to the overall length of the duplexes. In the referenced Figure 2, entitled "Diagram of Models for U insertion/deletion RNA editing", the overall length of the duplex structure is not taught, nor is the length of the region of complementarity. Specifically, an oligoribonucleotide consisting of a double stranded structure, wherein the structure is not more than 49 nucleotides in length, as encompassed by the instant claims, is not taught by Alfonzo et al.

Therefore, Alfonzo et al. cannot anticipate the oligoribonucleotides recited in the instant claims because Alfonzo et al. does not teach each and every claim limitation of the instant claims, by virtue of its not teaching: an oligoribonucleotide consisting of a double stranded

structure of a defined length which is fully complementary to less than the full length of an RNA transcript of a mammalian target gene, and which specifically inhibits the expression of a mammalian target gene.

In view of these amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 221, 222, 223, 224, 225, 232, 233, 234, 235, 236, 237, 238, 239, 243, 245 and 248-251 were rejected under 102(e) as being anticipated by Kmiec et al. (U.S. Patent No. 6,537,046).

As in the Alfonzo et al. rejection, the Office Action states that "the term 'comprising' and 'having' means that any dsRNA that comprises a region that is complementary to an RNA transcript of a mammalian gene and the region is not more than 49 nucleotides anticipates the claimed product". Accordingly, Applicants have amended the base claims 221, 224, 232 and 237 to recite that the encompassed oligoribonucleotide consists of a dsRNA.

Applicants have also amended base claims 221, 232 and 237 to recite that the two strands of the dsRNA are self-complementary. Applicants note that independent claim 224 already recites the limitation that the two strands of the dsRNA are self-complementary. This amendment was made in order to more clearly differentiate the claimed invention from an embodiment of an oligonucleotide taught by Kmiec et al. referred to by Examiner Whiteman. The referenced embodiment taught by Kmiec et al., is an oligonucleotide in which the two strands are not fully complementary to each other. Specifically Kmiec et al. teaches that:

"A particularly preferred embodiment of this invention is a DMV wherein the two strands are not fully-complementary. Rather the sequence of one strand comprises the sequence of the target DNA to be modified, and the sequence of the alternative strand comprises the different, desired sequence that the user intends to introduce in place of the target sequence", (column 11, lines 1-10).

Because the instant claims, as amended, recite that the two strands of the dsRNA are self-complementary, Applicants submit that the instant claims do not read on the above-mentioned heterodimeric embodiment taught by Kmiec et al.

Applicants have also amended base claims 221 and 232 to recite that the self complementary double stranded structure is fully complementary to less than the full length of an RNA transcript of a mammalian target gene. Applicants note that independent claims 224 and 237 already recite the limitation that the dsRNA structure is fully complementary to less than the full length of an RNA transcript of a mammalian target gene. This amendment to Claims 221 and 232 was made in order to more clearly differentiate the claimed invention from another set of embodiments of an oligoribonucleotide taught by Kmiec et al. in which the two strands are self complementary to each other at every base and which must also contain at least one "mutator region". The mutator region differs in sequence from the target gene and therefore is not fully complementary to the target gene. Specifically, Kmiec et al. teaches:

"In the embodiments wherein the strands are complementary to each other at every nucleobase, the sequence of the first and second strands consists of at least two regions that are homologous to the target gene and one or more regions (the "mutator regions") that differ from the target gene and introduce the genetic change into the target gene. The mutator region is directly adjacent to homologous regions in both the 3' and 5' directions", (column 8, lines 26-34).

In contrast, the self-complementary oligoribonucleotide encompassed by the instant claims is fully complementary to the target gene and does not contain the Kmiec et al. mutator region in which the strands are complementary to each other at every nucleobase, but not fully complementary to the target gene. Therefore, Kmiec et al. does not anticipate the instant claims.

As discussed above, Applicants submit that by A) amending the claims to recite closed language, such as "consisting of" in the phrase "An oligoribonucleotide consisting of a double stranded structure" in place of the open language of "having" or "comprising", B) amending the instant claims so they recite that the two strands of the dsRNA are self-complementary, and C) amending the instant claims so they recite that the dsRNA is fully complementary to less than the full length of an RNA transcript of a mammalian target gene, the instant claims are clearly distinct from the oligonucleotides taught by Kmiec et al. As detailed above, Claim 249 has been cancelled by Applicants because it does not further limit newly amended claim 221.

In view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request reconsideration and withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

Date: 1/9/04

Name: Kathleen Williams
Registration No.: 34,380
Customer No.: 29933
Palmer & Dodge LLP
111 Huntington Avenue
Boston, MA 02199-7613
Tel. (617) 239-0100